CURRENT MEDICAL RESEARCH AND OPINION®
VOL. 22, NO. 2, 2006, 327-333

0300-7995
doi:10.1185/030079906X80620

ORIGINAL ARTICLE

Moxifloxacin versus levofloxacin for treatment of acute rhinosinusitis: a retrospective database analysis of treatment duration, outcomes, and charges

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Key words: Acute rhinosinusitis – Antibiotic therapy – Fluoroquinolones – Recurrence – Therapy duration – Treatment charges – Treatment failure

ABSTRACT

Objective: Antibiotics are clinically indicated for acute bacterial rhinosinusitis, but they may be prescribed inappropriately. This retrospective study examined how labeled recommendations for duration of moxifloxacin and levofloxacin treatment of acute bacterial rhinosinusitis compare with real-world practice, and compared the failure and recurrence rates, and associated charges.

Methods and main outcome measures: The PharMetrics Patient-Centric claims database was searched over a 3-year period for episodes of acute rhinosinusitis treated within 5 days with moxifloxacin or levofloxacin. The duration of antibiotic treatment prescribed was compared with the labeled recommendation. Failure rates (a second antibiotic claim to treat acute rhinosinusitis within 30 days of the first claim), recurrence rates (subsequent antibiotic claims to treat any rhinosinusitis more than 30 days after the original or second [in the case of failure] claim), and treatment charges from the perspective of the payer (health insurer) were also compared using multivariate analysis.

Results: The initial duration prescribed of moxifloxacin was shorter than for levofloxacin (−1.65 days, $p < 0.0001$), reflecting the shorter labeled recommendation (10 days versus 10–14 days). The durations of monotherapy (−2.06 days, $p < 0.0001$) and of all antibiotic treatment (−1.97 days, $p < 0.0001$) were also significantly shorter for episodes treated initially with moxifloxacin. The odds ratio for treatment failure (0.718; 95% confidence interval = 0.598–0.863; $p = 0.0004$) and the hazard ratio for recurrence (0.652; $p = 0.0005$) were both significantly lower for moxifloxacin than for levofloxacin, and resulted in lower total treatment charges (−$37.94 ± 13.65; $p = 0.0055$).

Conclusion: The shorter treatment durations seen for moxifloxacin in this database of real-world care reflect the label-recommended duration for acute rhinosinusitis. Despite this shorter duration of therapy, moxifloxacin resulted in better outcomes than levofloxacin in terms of the risk of treatment failure and recurrence. In addition, the total charges were lower for patients treated with moxifloxacin.

Introduction

Rhinosinusitis is one of the ten most common conditions seen in the ambulatory setting in the USA, with an estimated 14% of the population suffering from the condition each year[1,2]. Rhinosinusitis results in over 15 000 000 physician office visits, 156 000 hospital inpatient days and over 45 000 hospital discharges annually[3], and has a significant effect on patient functional status, well-being and quality of life[4]. The overall healthcare expenditures attributable to rhinosinusitis in 1996 were estimated as $5.8 billion, of which $3.5 billion represented the direct expenditure related to a primary diagnosis of acute or chronic rhinosinusitis[3]. It has been estimated that Americans spend about $2.2 billion each year on prescription and over-the-counter drugs to treat viral and bacterial acute rhinosinusitis[5]. In 2002, 21% of all adult antibiotic prescriptions were for rhinosinusitis, making this condition the fifth most common condition for which an antibiotic is prescribed[6].

Acute rhinosinusitis is a condition characterized by infection and inflammation of the nose and paranasal sinuses[7]. It may be viral or bacterial in origin, and these two underlying causes are difficult to differentiate because their clinical features are similar[6], and non-bacterial rhinosinusitis may predispose a patient to a secondary bacterial sinus infection[8]. Viral respiratory infections are complicated by secondary bacterial infections in 0.5–2% of cases[1]. Because it is difficult to diagnose accurately, the exact incidence of acute bacterial rhinosinusitis is unknown, but an annual incidence of 20 million cases has been estimated[1]. The most common causative organisms of acute bacterial rhinosinusitis are *Streptococcus pneumoniae*, found in 20–43% of cases and *Haemophilus influenzae*, found in 22–35% of cases; *Moraxella catarrhalis* is also found in 2–10% of cases[6].

It is important to note that acute rhinosinusitis resolves spontaneously with no drug therapy in about 47% of cases[6]. However, when antibiotic therapy is indicated, the primary goal is not only to eradicate the causative bacteria, but also to reduce the underlying inflammatory process and return the sinuses to normal function; the decreased duration of symptoms allows patients to return to normal activities quickly, prevents complications, and decreases the risk of developing chronic sinusitis[6]. To meet this goal, appropriate therapies that provide quick resolution of symptoms with a low risk of recurrence are desirable, as they may reduce overall costs while providing rapid improvements in quality of life and return to normal functioning.

The Sinus and Allergy Health Partnership has developed guidelines to assist prescribers in antibiotic treatment choices when acute bacterial rhinosinusitis is suspected[6]. These recommendations classify patients into two broad groups on the basis of disease severity and prior antibiotic use and suggest appropriate treatment strategies for each. For adult patients with mild disease who have not received antibiotics in the past 4–6 weeks, the recommended treatment is amoxicillin/clavulanate, amoxicillin, cefpodoxime proxetil, cefuroxime axetil, or cefdinir, with trimethoprim/sulfamethoxazole, doxycycline, azithromycin, clarithromycin, erythromycin, or telithromycin as alternatives for patients with β-lactam allergies (though failure rates of up to 25% are possible with these drugs). For adult patients with mild disease who have received antibiotics in the past 4–6 weeks or adults with moderate disease, the recommended antibiotics are respiratory fluoroquinolones (gatifloxacin, moxifloxacin, or levofloxacin) or high-dose amoxicillin/clavulanate, which all appear to be equally effective[6]. Moxifloxacin has been shown to have immunomodulatory and anti-inflammatory effects[9,10], which may be a useful adjunct to its antibacterial effects.

Even when antibiotics are clinically indicated, they are often prescribed and used inappropriately. For example, research has shown that physicians sometimes prescribe a broad-spectrum antibiotic when a more specific one is required, or may prescribe the correct antibiotic in the wrong dose or for the wrong duration, which may lead to subsequent treatment failure and the possible emergence of resistant organisms[11,12]. A large, retrospective database analysis was undertaken to evaluate treatment patterns, incidence of treatment failures, and associated healthcare costs for outpatient management of several respiratory tract infections with commonly used fluoroquinolones and macrolides. This paper reports findings on how labeled recommendations for the duration of moxifloxacin and levofloxacin therapy in acute bacterial rhinosinusitis (10 days and 10–14 days, respectively) compare with real-world practice for treatment duration, and on comparisons of resulting failure and recurrence rates and associated charges.

Methods

This retrospective claims database analysis was performed using data from the PharMetrics Patient-Centric Database. The database contains data from at least 75 different US health plans, containing demographic information and medical and pharmaceutical claims for more than 55 million covered lives with over two billion healthcare transactions, including prescriptions, office visits, hospital stays, and diagnostic tests[13]. It includes inpatient (through submissions of the universal billing form UB-92) and outpatient diagnoses

and procedures, retail pharmacy and mail order prescription records, and data on Medicare Risk patients.

The section of the database analysis reported here used two random samples of 40000 patients each, aged ≥ 18 years, with at least 1 year of continuous enrollment during the period March 1999 to March 2002 and at least one prescription claim during that time for moxifloxacin or levofloxacin. Patients must not have had the alternate antibiotic within 30 days prior to the first script for the antibiotic of interest.

Inclusion and exclusion criteria for treatment episodes

Treatment episodes for analysis were selected by first identifying all office or hospital outpatient visits with an ICD-9 diagnosis of acute rhinosinusitis (ICD-9-CM 461.xx) between April 1, 2000 and March 31, 2002. Next, all of the episodes for which either moxifloxacin or levofloxacin was prescribed within 5 days of the rhinosinusitis diagnosis were identified. For each visit, the episode index date was defined as the date of diagnosis of acute rhinosinusitis. Moxifloxacin or levofloxacin was considered first-line therapy if there were no other antibiotic claims 30 days prior to the episode index date. The date of prescription filling was designated the drug index date and was the first day of the treatment episode. The end of the treatment episode was defined as 30 days after the drug index date or 30 days after the date of treatment failure for episodes with a treatment failure. The database was searched for all further episodes of rhinosinusitis (acute or chronic) after the initial episode, until no further treatment episodes were identified.

Treatment episodes were excluded if the antibiotic dose was missing; if the patient did not have continuous enrollment in the health plan for 180 days before and 30 days after each episode index date; if the episode started before 1 April 2000 or ended after 28 February 2002; if prescriptions for more than one of the study antibiotics were filled on the first day of the treatment episode or a prescription for an antibiotic other than moxifloxacin or levofloxacin was filled on the first day followed later by moxifloxacin or levofloxacin; if there was a claim relating to a diagnosis of upper respiratory tract infection or other respiratory infection on or up to 30 days before the first day of the treatment episode; if the patient was hospitalized on the first day of the treatment episode after filling the prescription; if there was any antibiotic prescription, office visit or hospitalization within 30 days prior to the episode index date; or if a patient had a diagnosis or underwent procedures indicative of a non-respiratory, antibiotic-treatable infection on or the day before the first day of the treatment episode.

Definitions of endpoints

Seven endpoints were studied, of which the first three focused on treatment duration as a measure of real-world practice. The duration of the original prescription measured the total number of days of therapy prescribed to the patient for the initial treatment episode. The duration of monotherapy measured the total number of days supplied of either moxifloxacin or levofloxacin among patients who had no treatment failure on the original prescription or who had a treatment failure defined as a refill of the original antibiotic prescription. The duration of all antibiotic therapy measured the total number of non-overlapping days supplied to the patient of moxifloxacin or levofloxacin, other oral or injectable antibiotics for treatment of acute rhinosinusitis (i.e., associated with failure), and days hospitalized for rhinosinusitis (assuming that antibiotic treatment was received every day of hospitalization).

Two endpoints focused on the outcomes of treatment for rhinosinusitis. Treatment failure was defined as the patient having, within 30 days of the drug index date, a drug claim for an oral or injectable antibiotic (other than the initial drug claim) used to treat acute rhinosinusitis with no other ICD-9 code indicating any other type of infection, or an inpatient claim with an acute rhinosinusitis diagnosis. Second or subsequent episodes of rhinosinusitis (with any rhinosinusitis diagnosis code) that occurred more than 30 days after the drug index date (or in the case of treatment failure, more than 30 days after the second antibiotic prescription was filled) were defined as recurrence.

Finally, two endpoints focused on charges. The total treatment charge was the sum of all treatment charges submitted to the health insurer that were incurred during the treatment episodes attributable to acute rhinosinusitis. These included: inpatient and outpatient facility claims; professional services claims, including injectable antibiotics and acute rhinosinusitis-related procedures; and outpatient pharmacy claims, including moxifloxacin and levofloxacin or any other antibiotic used to treat acute rhinosinusitis associated with a treatment failure. Outpatient pharmacy charges were also analyzed separately. Charges were adjusted to 2002 dollars using the Consumer Price Index.

Statistical analyses

Descriptive analyses, including means and standard deviations, were performed for continuous data, while distribution analysis was performed for categorical data. Additionally, for descriptive recurrence information, incidence density (defined as the number of first

recurrences per person–month of follow-up in the database) was calculated. Logistic regression was used to evaluate the odds of treatment failure between treatment episodes initiated with moxifloxacin versus levofloxacin. Ordinary least-squares regression was used to test for differences between treatment episodes initiated with moxifloxacin versus levofloxacin in the duration of all antibiotic therapy, the duration of moxifloxacin or levofloxacin monotherapy, and acute rhinosinusitis-associated charges. Proportional hazard regression was used to test for differences in the recurrence rates on treatment with moxifloxacin versus levofloxacin; this standard method eliminated the need to define a fixed time window for recurrence and accounted for patients who no longer appeared in the database before the end of the study.

All regression models controlled for potential covariates selected to control for the severity of acute rhinosinusitis and the patient's overall severity of illness. These covariates were age, gender, history of diabetes, history of a compromised immune system, acute steroid use, Charlson–Deyo co-morbidity score[14,15], log-lagged charges, and initial presentation to an emergency department. A history of diabetes was defined as the patient having two or more claims with a diagnosis of diabetes or a claim for an antidiabetic medication in the period beginning 180 days prior to the start of the treatment period and ending on the last day of the treatment period. Patients were considered to have a history of a compromised immune system if they had a claim with a diagnosis consistent with a compromised immune system in the period beginning 180 days prior to the start of the treatment period and ending on the last day of their most recent treatment period. Acute corticosteroid use was defined as the patient having no steroid use in the 180 days prior to the treatment episode, and then having corticosteroid use within 15 days of the acute rhinosinusitis episode index date. The Charlson–Deyo co-morbidity score is based on the number and severity of co-morbidities, with different weights assigned to various diagnoses[14,15]. Lagged charges were computed as the sum of charges from all facility, professional service, and outpatient claims that occurred in the 180 days prior to the office or emergency room service that initiated the treatment episode; the natural logarithm of these charges was used as a variable in the regression analyses in order to minimize the impact of outliers. For episodes with no lagged charges, the natural logarithm of $0.10 was used.

For each variable included in the regression analyses, univariate analysis was applied to identify differences between treatment periods on moxifloxacin or levofloxacin. Significance was determined using the Pearson chi-square test (exact values) for binary variables, the *t*-test for age, treatment duration and log-transformed charges, and the Wilcoxon non-parametric test for actual charges.

Results

In all, 3358 episodes of acute rhinosinusitis were identified with moxifloxacin as the initial therapy and 1522 episodes with levofloxacin as the initial therapy. The baseline characteristics of the patients who experienced these episodes were generally similar between the two groups (Table 1). The overall prevalence of diabetes in both groups was low, but was similar in both the moxifloxacin and levofloxacin groups. There were significant differences between the moxifloxacin and levofloxacin groups in the proportion

Table 1. Patient characteristics at baseline

	Moxifloxacin	Levofloxacin	*p* value
Number of episodes	3358	1522	
Demographics			
Male (% of patients)	32.3	32.2	0.93
Mean age (years ± SD)	43.9 ± 10.8	44.2 ± 10.9	0.36
Clinical characteristics			
Diabetes (%)	4.8	4.9	0.88
Compromised immune history (%)	24.8	28.7	0.003
Emergency room episodes (%)	0.1	0.5	0.008
Acute corticosteroid use (%)	4.9	5.1	0.75
Charlson–Deyo co-morbidity score (%)			
0–1	98.4	98.2	
2–3	1.5	1.6	
4–5	0.1	0	
6+	0	0.3	
Mean ± SD	0.07 ± 0.35*	0.08 ± 0.45*	0.66

*The standard deviations are much larger than the mean values because most patients had a co-morbidity score of 0

of patients with a compromised immune history and the proportion of episodes beginning in an emergency department.

The mean duration of therapy in the moxifloxacin group was significantly shorter than in the levofloxacin group (Table 2). After controlling for potentially confounding variables, the duration of the original prescription was significantly shorter by 1.65 days for the moxifloxacin group compared with the levofloxacin group. Both the other measures of duration (monotherapy duration and duration of all antibiotics) were also significantly shorter in the episodes treated initially with moxifloxacin than in those treated initially with levofloxacin.

The failure rate within 30 days of the drug index date was significantly lower in the moxifloxacin group compared with the levofloxacin group (10.0% versus 13.9%, $p = 0.0003$). After controlling for potential confounding variables, the odds of treatment failure were lower for the moxifloxacin group compared with the levofloxacin group (odds ratio = 0.718, 95% confidence interval = 0.598–0.863, $p = 0.0004$).

The overall recurrence rate (episodes occurring more than 30 days after the drug index date or more than 30 days after the date of filling a second prescription in the case of failure) was 6% for episodes preceded by an initial prescription for moxifloxacin and 9% for episodes preceded by an initial prescription for levofloxacin (odds ratio = 1.609, 95% confidence interval = 1.277–2.028; $p < 0.0001$) (Figure 1). The incidence density for recurrence was significantly lower in the moxifloxacin group than in the levofloxacin group (Table 3). Proportional hazard modeling, which controlled for confounding variables and for the time to recurrence, indicated that the probability of recurrence was 30–35% lower for episodes treated with moxifloxacin versus those treated with levofloxacin (Table 3), and this trend was apparent within 100 days of the end of the first episode.

The mean total charge per episode and the mean pharmacy charge per episode were significantly lower for episodes treated with moxifloxacin than for those treated with levofloxacin (Table 4). The log-lagged charges at baseline were also significantly lower in the

Table 2. Duration of therapy

	Moxifloxacin	Levofloxacin	*p* value	*F* statistic (*p* value)	R^2
Mean duration of initial therapy (days supplied ± SD)	10.4 ± 4.7	12.4 ± 5.4	< 0.001		
Difference in duration (days supplied ± SEM)*					
Original prescription	−1.65 ± 0.12		< 0.0001	26.59 (< 0.0001)	0.047
Monotherapy	−2.06 ± 0.15		< 0.0001	26.75 (< 0.0001)	0.049
All antibiotics	−1.97 ± 0.15		< 0.0001	22.67 (< 0.0001)	0.040

*Determined relative to levofloxacin by ordinary least-squares regression, controlling for diabetes, compromised immune history, log-lagged charges, start of an episode in the emergency department, acute steroid use, gender, Charlson–Deyo co-morbidity score and age

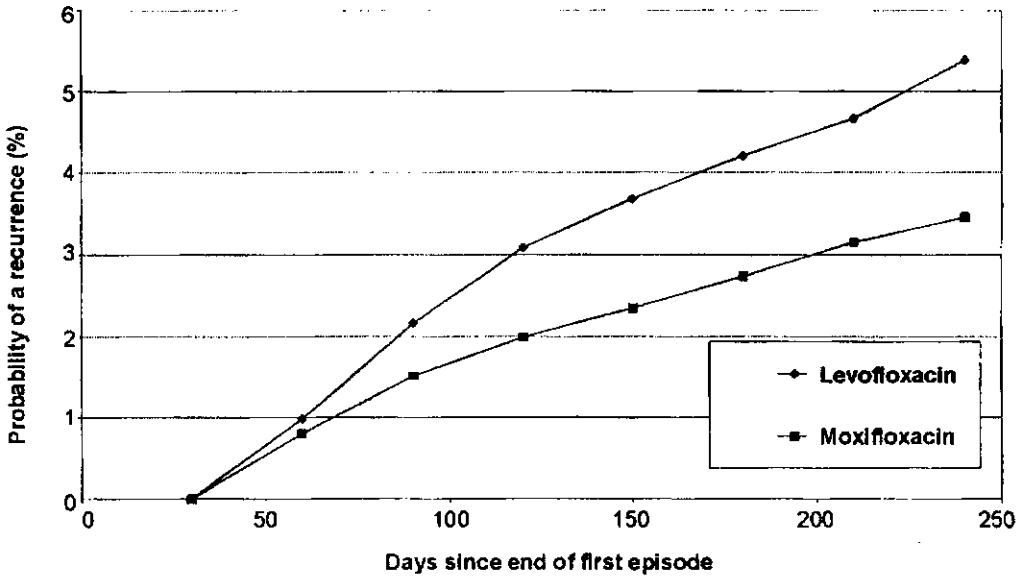

Figure 1. Recurrence of rhinosinusitis over time for all patients enrolled in the study

moxifloxacin group. After controlling for potentially confounding variables, the charges for treatment were significantly lower by nearly $40 per episode for moxifloxacin-treated episodes than for levofloxacin-treated episodes.

Discussion

Historically, antibiotic dosing has been stated as a range – often 7–14 days, or 10–14 days – leaving duration of therapy open to the physician's judgment. This study compares two fluoroquinolones commonly used to treat acute rhinosinusitis and indicates that the labeled recommendations for duration of therapy (10 days for moxifloxacin and 10–14 days for levofloxacin) are largely followed in real-world practice, and result in a shorter duration of use of moxifloxacin compared with levofloxacin. Despite this shorter duration of therapy, the moxifloxacin group experienced better outcomes (significantly fewer treatment failures and fewer recurrences) than the levofloxacin group with significantly lower charges for treatment.

The possibility that the benefits seen in the moxifloxacin group over the levofloxacin group in the descriptive analyses could have been due to the imbalances in the baseline characteristics (specifically, that the levofloxacin group had a significantly greater proportion of patients with a compromised immune history, more episodes starting in the emergency department, and greater log-lagged charges, i.e., were less sick) was eliminated by the regression analyses. In these analyses, which controlled for these and other potential confounding variables, the risk of failure or recurrence and the charges for treatment were still significantly lower in the moxifloxacin group compared with the levofloxacin group. It should be noted, however, that the definition used for a treatment episode excluded episodes of acute rhinosinusitis where the patient was also being treated for another antibiotic-treatable condition, and the overall recurrence rate may, therefore, have been underestimated.

A number of limitations in this study should be noted, related to using a claims database as the primary source of information. In particular, there are always concerns of missing data and miscoding, especially as there is often confusion between acute rhinosinusitis and chronic rhinosinusitis, and between bacterial and viral rhinosinusitis. Although only about 1 in 8 patients presenting with signs and symptoms of an upper respiratory tract infection has acute bacterial rhinosinusitis, family physicians prescribe antibiotics in up to 98% of suspected cases[7]. This would tend to decrease the apparent success rate of therapy, though this may be offset by the natural tendency of viral rhinosinusitis to resolve spontaneously. Claims found in the database represent services and products that were billed, which are not necessarily indicative of what patients actually received. Some prescriptions for antibiotics may have been written and never filled, while others may have been filled but not taken by the patient, and there is no way to capture such non-compliance. Samples of drugs given to patients in the physician's office may affect the duration of use captured in the dataset, but again this cannot be

Table 3. Recurrences

	Moxifloxacin	Levofloxacin	*p* value	Estimate ± SEM*	Hazard ratio*
Incidence density for recurrence of any rhinosinusitis (recurrence/person–month)	0.0050	0.0073	0.0072		
Recurrence of any rhinosinusitis*			0.0005	–0.428 ± 0.123	0.652

*Determined relative to levofloxacin by proportional hazard regression, controlling for diabetes, compromised immune history, log-lagged charges, start of an episode in the emergency department, acute steroid use, gender, Charlson–Deyo co-morbidity score and age

Table 4. Charges for treatment

	Moxifloxacin	Levofloxacin	*p* value	*F* statistic (*p* value)	R^2
Mean total charge per treatment episode ($ ± SD)	171.4 ± 231.0	211.5 ± 713.3	0.03		
Mean total pharmacy charge per treatment episode ($ ± SD)	103.0 ± 57.6	116.9 ± 65.2	< 0.0001		
Log-lagged charges at baseline ($)	6.17	6.39	0.008		
Difference in treatment charges ($ ± SEM)*	–37.94 ± 13.65		0.0055	5.12 (< 0.0001)	0.009
Difference in log of treatment charges ($ ± SEM)*	–0.093 ± 0.019		< 0.0001	23.26 (< 0.0001)	0.041

*Determined relative to levofloxacin by ordinary least-squares regression, controlling for diabetes, compromised immune history, log-lagged charges, start of an episode in the emergency department, acute steroid use, gender, Charlson–Deyo co-morbidity score and age

accounted for. Unfortunately, there is no way of assessing the impact of these limitations on the study's findings.

The regression models did not include use of other antibiotics as monotherapy or co-administered with either moxifloxacin or levofloxacin as the definition of the initial treatment episode excluded such antibiotic use. Although the severity of the acute rhinosinusitis cannot be determined from the claims database, the variables selected for the regression analyses to some extent control for severity and for the patient's overall state of health, which may influence the severity of the infection. However, the regression models explained less than 5% of the variance, and it is thus likely that other (unmeasured) variables would improve the fit.

In determining which fluoroquinolone to use for patients presenting with moderate acute rhinosinusitis or with mild acute rhinosinusitis with a history of recent antibiotic use, it is helpful for physicians to consider the clinical efficacy and real-world effectiveness of different members of this group. Practitioners must also consider the prevalence and risk of antibiotic resistance in their community before prescribing an antibiotic. One of the strengths of this study is that the effectiveness data came from a cohort of patients in a naturalistic setting. The claims for treatment also represent the real charges made for treatment. These charges, from the perspective of the payer, can be considered as a proxy for costs; this is often done by applying a standard fee schedule to the claims data, e.g., based on the Centers for Medicare and Medicaid Services resource-based relative value scale standards and median billed charges, which minimizes the influence of capitation and contractual agreements on the claim charges. The charges thus provide an estimate of the costs incurred for the different antibiotics and associated healthcare provision by the health insurance plans, i.e., the payers, contributing to the database.

Conclusions

It appears that the labeled recommendations for antibiotic treatment duration for acute rhinosinusitis are followed when moxifloxacin and levofloxacin (10 days and 10–14 days, respectively) are used in real-world practice. Despite this shorter duration of therapy, moxifloxacin resulted in better outcomes than levofloxacin in terms of the risks of treatment failure and recurrence. In addition, the total charges were lower for those patients treated with moxifloxacin. This study suggests that moxifloxacin may be preferable to levofloxacin when a fluoroquinolone is used for the treatment of acute rhinosinusitis.

Acknowledgments

Funding for this research was provided by Bayer Pharmaceuticals, Inc.

The authors would like to acknowledge the contributions of Ashley Slagle MS, University of Maryland School of Pharmacy, Baltimore, MD, USA.

References

1. Meltzer EO, Szwarcberg J, Pill MW. Allergic rhinitis, asthma, and rhinosinusitis: diseases of the integrated airway. J Manag Care Pharm 2004;10:310-7
2. Gooch 3rd WM. Antibacterial management of acute and chronic sinusitis. Manag Care Interface 1999;12:92-4
3. Ray NF, Baraniuk JN, Thamer M, et al. Healthcare expenditures for sinusitis in 1996: contributions of asthma, rhinitis, and other airway disorders. J Allergy Clin Immunol 1999;103:408-14
4. Piccirillo JF. Acute rhinosinusitis: staging, diagnosis/outcomes assessment. Infect Med 1998;15:16-25
5. Benninger MS, Sedory Holzer SE, Lau J. Diagnosis and treatment of uncomplicated acute bacterial rhinosinusitis: summary of the Agency for Health Care Policy and Research evidence-based report. Otolaryngol Head Neck Surg 2000;122:1-7
6. Anon JB, Jacobs MR, Poole MD, et al. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol Head Neck Surg 2004;130(Suppl 1):1-45
7. Scheid DC, Hamm RM. Acute bacterial rhinosinusitis in adults: part I. Evaluation. Am Fam Phys 2004;70:1685-92
8. Ferguson BJ. Acute and chronic sinusitis: how to ease symptoms and locate the cause. Postgrad Med 1995;97:45-57
9. Shalit I, Horev-Azaria L, Fabian I, et al. Immunomodulatory and protective effects of moxifloxacin against Candida albicans-induced bronchopneumonia in mice injected with cyclophosphamide. Antimicrob Agents Chemother 2002;46:2442-9
10. Weiss T, Shalit I, Blau H, et al. Anti-inflammatory effects of moxifloxacin on activated human monocytic cells: inhibition of NF-kappaB and mitogen-activated protein kinase activation and of synthesis of proinflammatory cytokines. Antimicrob Agents Chemother 2004;48:1974-82
11. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database of Systematic Reviews, available from www.de.cochrane.org/review/en/ab003539.html [last accessed 15 November 2005]
12. Guillemot D, Carbon C, Vauzelle-Kervroëdan F, et al. Inappropriateness and variability of antibiotic prescribing among French office-based physicians. J Clin Epidemiol 1998;51:61-8
13. PharMetrics Overview. Available from http://www.pharmetrics.com/h_overview.html [last accessed 14 November 2005]
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:73-83
15. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613-9

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Paper CMRO-3237_3, *Accepted for publication*: 06 December 2005
Published Online: 11 January 2006
doi:10.1185/030079906X80620